

# Hemispheric-synchronisation during anaesthesia: a double-blind randomised trial using audiotapes for intra-operative nociception control

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## Summary

The possible antinociceptive effect of hemispheric-synchronised sounds, classical music and blank tape were investigated in patients undergoing surgery under general anaesthesia. The study was performed on 76 patients, ASA 1 or 2, aged 18–75 years using a double-blind randomised design. Each of the three tapes was allocated to the patients according to a computer-generated random number table. General anaesthesia was standardised and consisted of propofol, nitrous oxide 66%/oxygen 33%, isoflurane and fentanyl. Patients breathed spontaneously through a laryngeal mask and the end-tidal isoflurane concentration was maintained near to its minimum alveolar concentration value of 1.2%. Fentanyl was given intravenously sufficient to keep the intra-operative heart rate and arterial blood pressure within 20% of pre-operative baseline values and the fentanyl requirements were used as a measure of nociception control. Patients to whom hemispheric-synchronised sounds were played under general anaesthesia required significantly less fentanyl compared with patients listening to classical music or blank tape (mean values: 28 µg, 124 µg and 126 µg, respectively) ( $p < 0.001$ ). This difference remained significant when regression analysis was used to control for the effects of age and sex.

**Keywords** Classical music, general anaesthesia, Hemi-Sync, intra-operative awareness, nociception.

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Intra-operative awareness during general anaesthesia has been of concern to anaesthetists since the beginnings of modern anaesthetic practice [1]. The incidence of intra-operative awareness without nociception has been estimated at 2/1000 operations, and the incidence of intra-operative awareness with nociception at 1/10000 operations [2]. Conscious awareness without explicit recall, however, may be a much more common accompaniment of anaesthesia [2, 3]. Several studies have examined the possibility of using this phenomenon to benefit the patient but these have produced conflicting results. Some studies found that positive verbal suggestions [4–6], sounds of the sea [7], music [8], or a combination of these [7], improved intra-operative relaxation and postoperative recovery but others could not replicate these findings [9–11].

A new approach which aims to make therapeutic use of intra-operative awareness is described in the Surgical Support Series of the Monroe Institute in Virginia, USA. This advocates the use of hemi-synchronised sounds in combination with positive verbal suggestions [12]. Hemi-synchronised sounds are generated by binaural beats, which were discovered in 1841 by the German Professor of Physics, Heinrich Wilhelm Dove [13]. These occur when two coherent sounds of nearly similar frequencies are presented to each ear simultaneously. The brain detects phase differences between these sounds which under normal circumstances provide it with directional information. However, when binaural beats are presented to the listener with stereo headphones, the brain receives a different frequency from each ear and responds not by

hearing both frequencies but a 'third frequency', comprising the difference between the two. Perceived as a fluctuating rhythm at the frequency of the difference between the two stereo auditory inputs, binaural beats appear to originate in the brainstem's superior olivary nucleus, the site of contralateral integration of auditory inputs. This auditory sensation is neurologically routed to the reticular formation. At the same time the volume of the binaural beat is conducted to the cortex where it can be objectively measured as frequency-following response because its period, measured in cycles per second, corresponds to the fundamental frequency of the stimulus. This provides proof that the sensation of binaural beating has neurological validity [14].

It is known that certain sound patterns with binaural beats can induce states of consciousness which occur naturally only for random, very brief periods in daily life. This is known as hemispheric synchronisation (Hemi-Sync) because it brings both hemispheres of the brain into unison [15]. This can be demonstrated by computerised topographic brain-wave maps. Though there are many anecdotal reports about the effectiveness of Hemi-Sync for nociception control, no randomised controlled trial has yet been published which supports these claims. We planned a double-blind randomised controlled trial to compare the effects of Hemi-Sync sounds, classical music and a blank tape on nociception control in patients undergoing surgery under general anaesthesia.

## Patients and methods

During 1997, 76 unpremedicated patients, ASA 1 or 2, aged 18–76 years who were scheduled for general surgical operations under general anaesthesia at Queen Mary's Hospital, Sidcup, UK, were studied. Patients were not studied if they: disliked classical music; knew the Monroe Institute or knew about Hemi-Sync; suffered from a known malignancy; had a hearing impairment or were mentally impaired; used regular painkillers, tranquillisers or anti-hypertensive medicines; were known alcoholics or drug users; had a history of epilepsy or mental illness; were pregnant; were scheduled for operations involving the head or neck area; were not suitable for the standardised anaesthetic technique. The study was approved by the local Medical Ethics Committee and all patients gave their informed consent.

The estimated length of stay of each patient in hospital was determined by the surgeon. On arrival in the anaesthetic induction room, one of three numbered but unlabelled tapes was randomly assigned to the patient by computer-generated random number table. The randomisation was stratified according to the estimated length of stay (less than 2 days and more than this). The tape was

inserted into the cassette player by a person other than the anaesthetist; both at this point and throughout the study, the anaesthetist remained unaware of the nature of the tape. Following induction of anaesthesia with propofol  $2.5 \text{ mg.kg}^{-1}$ , a laryngeal mask was inserted and the patient was connected to an anaesthetic breathing system (Engström EAS 9010 or Ohmeda Excel 210 SE machines). When anaesthesia was stable, a pair of headphones was positioned over the patient's ears and the cassette player set to 'Play'. The tape played continuously until the end of surgery.

The patient breathed isoflurane in 33% oxygen and 66% nitrous oxide and the pre-operatively recorded heart rate and arterial blood pressure were used as guides for the required inspired isoflurane concentration. The objective was to keep the intra-operative heart rate and arterial blood pressure within the pre-operative limits and thereby to use the smallest amount of isoflurane possible up to an MAC of 1.2% end-tidal concentration. The ECG was monitored continuously and recorded at 1-min intervals and the blood pressure was recorded noninvasively every 5 min. If the intra-operative blood pressure or heart rate increased by 20% or more above baseline values for more than 5 min, fentanyl was given intravenously until the baseline was attained and the dose of fentanyl was recorded. Thus, the fentanyl requirement served as an indication of the adequacy of nociception control provided during the operation.

## Tape methods

In order to compare the effects of the continuous Hemi-Sync sounds with non-Hemi-Sync sounds, two control groups were used. One group listened to a tape of quiet classical music ('Adagio' Karajan, Deutsche Grammophon, 445 282-4) and the other group listened to a blank tape (BASF reCorDII Chrome) which was perceived as silent. The tapes were played on a stereo cassette player (Aiwa HS-PX347) with a fixed output of 6 mW from each stereo channel, and sound-attenuated stereo headphones (Panasonic RP-HT240) were used.

## Statistical analysis

Data were entered using Microsoft Excel 7.0, and SPSS 7.5, for Windows. Kruskal–Wallis tests were used to compare subgroups of patients. The means were compared using the *F*-test and regression analysis to control for the effects of age and sex. Statistical significance was assumed at *p* levels of  $<0.05$ .

## Results

In total, 92 patients fulfilled the eligibility criteria and were invited to participate in the study. Eighty-three of these

**Table 1** Patient characteristics.

	Tape group		
	Blank	Classical	Hemi-Sync
<i>Men/women</i>	9/17	9/16	15/10
<i>Women</i>			
Age; years mean (SD) [range]	49 (11.5) [28–72]	48 (16.2) [24–75]	49 (12.6) [25–62]
Body mass index; kg.m <sup>-2</sup>	17.6–30.5	18.4–33.1	20.3–32.7
<i>Men</i>			
Age; years mean (SD) [range]	43 (19.9) [21–75]	50 (9.9) [33–64]	37 (15.6) [18–74]
Body mass index; kg.m <sup>-2</sup>	21.2–38.8	21.2–29.3	21.2–30.9

Hemi-Sync: hemispheric synchronised sound.

gave their informed consent but seven later revoked this in the induction room. Thus, 76 patients participated in the study. Table 1 shows the patient characteristics for each treatment group. The operations consisted of lump removal, stripping and avulsion of varicose veins, hernia repair, haemorrhoidectomy, arthroscopy, open reduction and internal fixation of bones and joints, vaginal hysterectomy and vaginal repair. The overall pre-operative mean baseline haemodynamic values were: heart rate 72 beat.min<sup>-1</sup>; systolic blood pressure 127 mmHg; diastolic blood pressure 78 mmHg. The mean (SD) durations of the operation were 48 (28), 53 (42) and 63 (41) min for the blank, classical and Hemi-Sync groups, respectively. Similarly, the mean (SD) intra-operative heart rates were 76 (14), 75 (14) and 75 (9) beat.min<sup>-1</sup>. The mean (SD) intra-operative maximum systolic blood pressures were 121 (12), 132 (24) and 129 (18) mmHg for blank, classical and Hemi-Sync groups, respectively ( $p = 0.090$ ) and the mean (SD) intra-operative maximum diastolic blood

**Table 2** Mean (SD) [95%CI] fentanyl requirements ( $\mu\text{g}$ ) in 76 patients hearing the tape recordings listed.

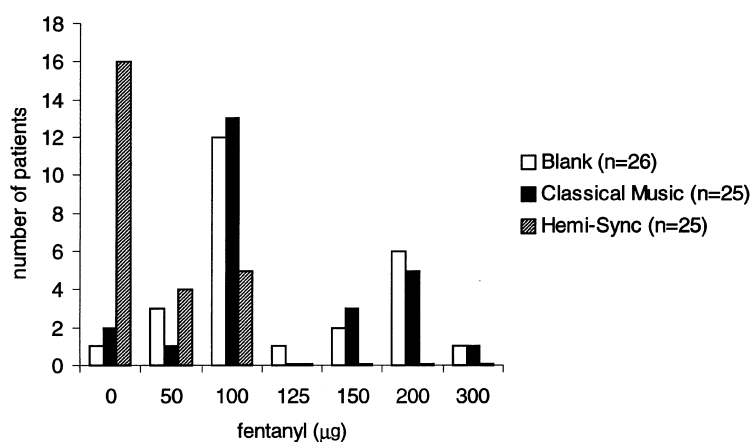
Blank ( $n = 26$ )	126 (65) [99.8–152.3]
Classical music ( $n = 25$ )	124 (66) [96.8–151.2]
Hemi-Sync ( $n = 25$ )	28 (41) [11.1–44.9]

Hemi-Sync: hemispheric synchronised sound.

pressures were 66 (17), 68 (14), and 66 (13) mmHg, respectively. The mean (SD) end-tidal isoflurane concentrations in the three groups were 1.0% (0.2) for blank tape, 1.0% (0.2) for the classical tape and 1.0% (0.2) for the Hemi-Sync tape.

Table 2 shows the mean fentanyl requirement of each of the study groups. Patients in the Hemi-Sync group required less fentanyl than both the classical music group (mean difference  $-96 \mu\text{g}$ , 95% confidence interval  $-64.6 \mu\text{g}$  to  $-127.4 \mu\text{g}$ ) ( $p < 0.001$ ) and the blank tape group (mean difference  $-98 \mu\text{g}$ , 95% confidence interval  $-67.4 \mu\text{g}$  to  $-128.6 \mu\text{g}$ ) ( $p < 0.001$ ). A comparison of the fentanyl requirements of each sex for the three treatment groups showed similar results. Figure 1 shows the distribution of fentanyl dosages for each of the study groups. None of the patients in the Hemi-Sync group required fentanyl dosages greater than 100  $\mu\text{g}$ . Patients in the blank tape and classical music groups required on average 4.5 times as much fentanyl as the patients in the Hemi-Sync group. This difference remained significant when regression analysis was used to control for the effects of age and sex (adjusted difference 96  $\mu\text{g}$ , SE 15  $\mu\text{g}$ ).

When these data are broken down into those patients with estimated length of stays of less than and over 2 days, the Hemi-Sync group still required significantly less fentanyl than the others ( $p < 0.001$  in both).

**Figure 1** Distribution of treatment group by fentanyl requirement in patients hearing the taped sounds listed. Hemi-Sync: hemispheric synchronised sound.

## Discussion

The phenomenon of intra-operative awareness was first described in 1847 [1], but opinion about its precise occurrence is conflicting. Some studies claim that hearing is the last of the senses to go before a patient loses consciousness and probably the first to return when consciousness is regained [16, 17], while others do not support this claim [18]. However, it has been shown that some patients continue to hear under general anaesthesia [17] even when a general anaesthetic is administered with opioids, benzodiazepines and volatile inhalation agents, and when intra-operative control parameters, such as heart rate and arterial blood pressure, remain within normal limits [3, 19]. Through preservation of the early cortical potentials of midlatency auditory evoked potentials, auditory information may be processed [20, 21], especially during 'light' anaesthesia [21, 22]. Modern investigations using pEEG (processed EEG) monitoring show that clinical signs, such as arterial blood pressure and heart rate, may be unreliable indicators of intra-operative awareness. Intra-operative pEEG analysis suggests that at the end of an operation the patient may be nearing consciousness some 2 min before this becomes apparent from the clinical signs [23].

In our study, we found that patients exposed to a Hemi-Sync audio tape whilst undergoing surgery under 'light' general anaesthesia required significantly less analgesia with fentanyl when compared with patients listening to a blank tape or to classical music. No significant differences in pain-relieving properties were observed between the classical music and the blank tape but the power of this study may have been inadequate to reveal such differences. Although no statistically significant differences were observed in mean duration of operation between the three study groups, on average the operations carried out in the Hemi-Sync group took longest, followed by the classical music group and the blank tape group. However, a longer duration of operation exposes the patient to a longer period of nociception requiring more fentanyl. Thus, any bias might be expected to reduce any observed effect of the nociception-relieving properties of the Hemi-Sync tape. Another potential source of bias in the study arises from the slightly higher (though not statistically significant) frequency of men in the Hemi-Sync group compared with the other groups. Though the widely held belief that women have a higher pain threshold than men has been reported [24], most studies either found no sex difference in pain perception [25] or reported a higher pain threshold for men than for women [26]. We were unable to detect any significant effect of gender on the doses of fentanyl required when our data were analysed both for all study patients and for the Hemi-Sync patients

alone. This suggests that the reported gender differences in pain reception at a conscious level do not exist for nociception.

We believe our findings could have important implications for anaesthetic practice, because they identify a new, environmentally friendly and effective method of intra-operative nociception control. It is possible that the Hemi-Sync tapes, used intra-operatively or with the addition of pre- and postoperative tapes, could have longer-term effects on postoperative recovery, and may even result in cost savings through reduced analgesic requirement and shorter hospital stay. Our findings also imply that patients may be able to hear under light general anaesthesia, which would be supported by the findings of some of the studies mentioned above. A pEEG could have ascertained more precisely the level of consciousness, but was beyond the resources available for this study.

In conclusion, our findings demonstrate that patients using intra-operative Hemi-Sync tapes whilst undergoing a range of different surgical procedures under standardised general anaesthesia with a laryngeal mask require substantially less fentanyl when compared with controls. On the basis of the preliminary findings of this pilot study, we believe that larger randomised studies are now required which utilise all the tapes in the Surgical Support Series. These studies should incorporate more precise monitoring of consciousness levels by pEEG, a comprehensive assessment of postoperative recovery and long-term outcomes, and a full economic evaluation.

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